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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,826	04/06/2006	Gerard Marx	2488.014	8215

23405 7590 03/08/2010

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EXAMINER	
AUDET, MAURY A	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
03/08/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,826	MARX ET AL.	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-14,20-25,31-41,43 and 48-51* is/are pending in the application.

4a) Of the above claim(s) *11-14,20-25,31-33,37-41,43,50 and 51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10,34-36,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 January 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The present application has been transferred from former Examiner Young to the present Examiner.

Applicant's response of 11/2/09 is acknowledged.

However, due to the new art of record uncovered under the updated search (Applicant's own prior work (nearly 3 years ago; 20 9961041), in combination with any reference (a few cited merely by example) on liposomes used with peptides, provides for motivation/predictability to use any liposome (or other increased cellular uptake promoter) with SEQ ID NO: 1; based on liposomes known function of increasing cellular uptake - as noted in the Double Patenting rejections of the previous Office Action. **The results Applicant has provided as assertedly 'unexpected' by adding liposomes to SEQ ID NO: 1 in composition, are wholly 'Expected', based on liposomes known use in increasing cellular uptake of compounds. The ONLY unexpected results scenario the Examiner can formulate for Applicant's consideration, is whether Applicant has unexpected shown one type of liposome to unexpected (and significantly) increase cellular uptake of SEQ ID NO: 1, versus other liposomes – after testing the former versus the latter.**

As noted in the last Office Action, the Examiner telephoned Applicant's representative to indicate the only outstanding issue [until now, new art necessitating a 35 USC 103 rejection] is the filing of a Terminal Disclaimer over at least the '620 patent. And to inquire if Applicant was interested in filing a Terminal Disclaimer over the '620 or any other patent claims that have issued from this family over products consisting of SEQ ID NO: 1. Applicant's representative thanked the Examiner but asked the present Office Action be sent in writing for consideration.

Election/Restrictions

As previously noted, Applicant's **election without traverse of Group I, original claims 1-10 and 34-36, as drawn to the elected peptide of the invention, a peptide consisting of SEQ ID NO: 1** in the reply filed on 7/10/07 is acknowledged.

Amended claims 11-14, 20-25, 31-41, 43, and new claims 50-51 are now withdrawn from consideration. **Claims 1, 7-10, 34-36 and new claims 48-49 have only been examined in so far as they read upon the elected peptide of the invention, a peptide consisting of SEQ ID NO: 1.**

In response hereto, Applicant is asked to the put the claims with their proper status identifier.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 7-10, 34-36, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9961041 (Hadasit Med Res Serv; two present inventors earlier work by nearly 3 years) in view of any of the following liposome + peptide references provided merely as examples of liposomes art-recognized function as cellular uptake promotors:

1. Slepian et al. (US 5843156)
2. Neilsen et al. (US 2002/0188101)
3. Spytek et al. (US 2003/0198953)
4. Tasset et al. (US 5,972,599)

At the outset, it is noted that the Examiner set forth and maintained the grounds of rejection under Double Patenting for the following substantive reasons:

> **Namely, the use of liposomes for increased cellular uptake of other compounds is a known result of the use of liposomes. [ ] Although the present application is to a "liposomal" compositions comprising SEQ ID NO: 1, compositions comprising liposomes need no reference for an introduction. The use of liposomes to carry e.g. other active agents, in combination with peptides has been well known in the art for over a decade a routinely used form of compositions. [ ] Regarding the previous recitation that absent evidence to the contrary that these specific liposomes carry some other unexpected property not routinely used within the peptide composition arts – which was not shown. Namely, the asserted unexpected property is liposomes known property – that they increase the cellular update of other compounds.**

These same reasons are applied under 35 USC 103 (Obviousness Double Patenting's prior art equivalent) based on Applicant's prior work to SEQ ID NO: 1 (labeled FITC-09) with cell attachment (sepharose beads)/cell membrane type molecules in composition with FITC-09.

WO 9961041 teach SEQ ID NO: 1 (labeled FITC-09) with cell attachment (sepharose beads)/cell membrane type molecules in composition with FITC-09. BUT, that took "prolonged exposure" for FITC-09 (once attached to the cell) to accumulate in the cytoplasm, and migrate to the pernicular areas and granular bodies. THUS, there was a gap between the CELLULAR BINDING provided by the attachment of FITC-09 to sepharose beads versus the rapidity of CELLULAR UPTAKE. However, it is art recognized that agents exist to aid cellular uptake, such as liposomes.

Mere examples of the latter's art recognition are provided in the following four (4) references:

1. Slepian et al. (US 5843156): col. 9, l. 2-6; Claims 10, 12, 14.

> "In most cases, it is possible to physically incorporate the bioactive agent by mixing with the material prior to application to the tissue surface and polymerization. The material can be mixed into the monomer solution to form a solution, suspension or dispersion. In one embodiment, the bioactive agent can be encapsulated within delivery devices such as microspheres, microcapsules, liposomes, cell ghosts or pseudovirions, which in themselves effect release rates and uptake by cells such as phagocytic cells."
>
> 10. The method of claim 9 wherein the haptotactic agent is an extracellular matrix protein.
>
> 12. The method of claim 11 wherein the haptotactic peptide is a cyclic peptide containing the RGD sequence.
>
> 14. The method of claim 11 wherein the haptotactic peptide contains the sequence YIGSR.

2. Neilsen et al. (US 2002/0188101): Claims 21 and 32.

> 21. A method of modulating cellular uptake and distribution of a peptide nucleic acid comprising the steps of: (a) conjugating said peptide nucleic acid with a lipophilic group; and (b) introducing the conjugated peptide nucleic acid of step (a) into liposomes.

32. A method of modulating cellular uptake and distribution of a peptide nucleic acid in a cell or tissue comprising administering to the cell or tissue a composition comprising a peptide nucleic acid incorporated into a liposome, said peptide nucleic acid having formula:

3. Spytek et al. (US 2003/0198953) : Para 393

"[0393] In another embodiment, PNAs of NOVX can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art."

4. Tasset et al. (US 5,972,599): col. 11, last para to col. 12; col. 16, lines 25-37

Brief Summary Text - BSTX (61):
Using in situ hybridization, RANTES expression has been found in interstitial mononuclear cells and proximal tubular epithelial cells in human kidney transplants undergoing rejection. Antibody staining revealed the presence of RANTES not only within the interstitial infiltrate and renal tubular epithelial cells but also in high abundance in inflamed endothelium (Wiedermann et al., 1993). Based on these results a haptotactic mechanism was postulated. Haptotaxis is defined as cell migration induced by surface-bound gradients. The haptotactic mechanism was supported by in vitro experiments and anti-RANTES antibodies have been found to prevent that in vitro haptotaxis.

Brief Summary Text - BSTX (87):
The nucleic acid ligands described herein can be complexed with a lipophilic compound (e.g., cholesterol) or attached to or encapsulated in a complex comprised of lipophilic components (e.g., a liposome). The complexed nucleic acid ligands can enhance the cellular uptake of the nucleic acid ligands by a cell for delivery of the nucleic acid ligands to an intracellular target. U.S. patent application Ser. No. 08/434,465, filed May 4, 1995, entitled "Nucleic Acid Ligand Complexes," which is incorporated in its entirety herein, describes a method for preparing a therapeutic or diagnostic complex comprised of a nucleic acid ligand and a lipophilic compound or a non-immunogenic, high molecular weight compound.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use lipsomes or like-kind cellular uptake promoters with SEQ ID NO: 1

as provided by any of the combinations above and the motivation/predictability provided; absence evidence to the contrary that – as the Examiner stated at the outset:

> **The results Applicant has provided as assertedly 'unexpected' by adding liposomes to SEQ ID NO: 1 in composition, are wholly 'Expected', based on liposomes known use in increasing cellular uptake of compounds. The ONLY unexpected results scenario the Examiner can formulate for Applicant's consideration, is whether Applicant has unexpected shown one type of liposome to unexpected (and significantly) increase cellular uptake of SEQ ID NO: 1, versus other liposomes – after testing the former versus the latter.**

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Double Patenting-Maintained For the Reasons of Record

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 1, 7-10, 34-36, and 48-49 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 7,122,620 (09/847,790), is maintained for the reasons of record.

The previous grounds are provided below for continuity of record:

Applicant's arguments have been considered but are not found persuasive. **Namely, the use of liposomes for increased cellular uptake of other compounds is a known result of the use of liposomes.** Thus, the use of a peptide "consisting of SEQ ID NO: 1" remains drawn to a product, namely another composition, of which nothing would have prevented the '620 product claims to the same peptide from being use therein, especially given the '620's composition open "comprising" transition phrase to any other known products/molecules being capable of use within the '620's composition.

As noted previously, although the conflicting claims are not identical, they are not patentably distinct from each other because the '620 patent is drawn to a peptide or any type of composition comprising identical SEQ ID NO: 1. **Although the present application is to a "liposomal" compositions comprising SEQ ID NO: 1, compositions comprising liposomes need no reference for an introduction. The use of liposomes to carry e.g. other active agents, in combination with peptides has been well known in the art for over a decade a routinely used form of compositions.**

Regarding the previous recitation that absent evidence to the contrary that these specific liposomes carry some other unexpected property not routinely used within the peptide composition arts – which was not shown. Namely, the asserted unexpected property is liposomes known property – that they increase the cellular update of other compounds.

The rejection of claims 1, 7-10, 34-36, and 48-49 as provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-20 of copending Application No. US 20070009571 (11/490,033), is maintained for the reasons of record.

The previous grounds are provided below for continuity of record:

As noted previously, although the conflicting claims are not identical, they are not patentably distinct from each other because the '571 claims 11-20 are drawn to compositions/products comprising SEQ ID NO: 1, identical to presently elected SEQ ID NO: 1, and elected products thereof. Although the present application is to a "liposomal" compositions comprising SEQ ID NO: 1, compositions comprising liposomes need no reference for an introduction. The use of liposomes to carry e.g. other active agents, in combination with peptides has been well known in the art for over a decade a routinely used form of compositions. Absent evidence to the contrary these specific liposomes carry some other unexpected property not routinely used within the peptide composition arts.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The rejection of claims 1, 7-10, 34-36, and 48-49 as provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of copending Application No.11/601,024 (US 20070066535), is maintained for the reasons of record.

The previous grounds are provided below for continuity of record:

As noted previously, although the conflicting claims are not identical, they are not patentably distinct from each other because the '024 claims 1-2 are drawn to a peptide/product comprising a peptide of at least 50-70% identity to the carboxy termini of fibrinogen. Read in light of the specification, SEQ ID NO: 14 meets the limitations of 1-2 of '024 and SEQ ID NO: 14 is identical to presently elected SEQ ID NO: 1, and elected products thereof. Although the present application is to a "liposomal" compositions comprising SEQ ID NO: 1, compositions comprising liposomes need no reference for an introduction. The use of liposomes to carry e.g. other active agents, in combination with peptides has been well known in the art for over a decade a routinely used form of compositions. Absent evidence to the contrary these specific liposomes carry some other unexpected property not routinely used within the peptide composition arts.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112 2nd-NEW

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7-10, 34-36, 48, and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In e.g. claim 1, the peptide of SEQ ID NO: 1 is described as a "haptotactic peptide". The term haptotactic is art-recognized as meaning "cell attaching". However, as claimed the metes and bounds of the claimed invention are unclear. Applicant's earlier work in WO 9961041 (nearly 3 years before this applications priority date), describe the binding of FITC-09 (present SEQ ID NO: 1) to sepharose beads (SB) in order to evaluate their adhesive properties (see e.g. page 13, 15, 22, 23). However, sepharose beads have not been positively claimed as required by the composition, in order to render SEQ ID NO: 1 "haptotactic". What evidence can Applicant provide that SEQ ID NO: 1 is "haptotactic" without attachment to sepharose beads? Should Applicant respond that it is, without evidence that it binds ALONE any more than any other peptide to its respective receptor - does this mean that ALL peptides are inherently "haptotactic"? And if so, isn't use of the term superfluous in the context of any peptide, including SEQ ID NO: 1?

Citation of Pertinent Art Not Relied Upon-Previously Provided

As previously noted, the prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Regarding the subject matter of haptotactic peptides, Applicant has one other issued patent, related, though drawn to distinct haptotactic peptides (all under examination by Examiners other than the present):

US 7,148,190 (10/181,187)

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 2/15/2010

/Maury Audet/
Primary Examiner, Art Unit 1654